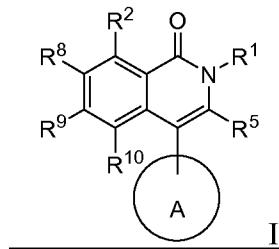


## AMENDMENTS TO THE CLAIMS

Claims 1-6 (canceled)

7 (Currently Amended)

A compound of the structure:



or a pharmaceutically acceptable salt, crystal form, or hydrate, wherein:

A is

a) an aryl ring, wherein any stable aryl ring atom is independently unsubstituted or substituted with

- 1) halogen,
- 2) NO<sub>2</sub>,
- 3) CN,
- 4) CR<sup>46</sup>=C(R<sup>47</sup>R<sup>48</sup>)<sub>2</sub>,
- 5) C≡C R<sup>46</sup>,
- 6) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>OR<sup>46</sup>,
- 7) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>N(R<sup>46</sup>R<sup>47</sup>),
- 8) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>C(O)R<sup>46</sup>,
- 9) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>C(O)OR<sup>46</sup>,
- 10) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>R<sup>46</sup>,
- 11) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>S(O)O-2R<sup>61</sup>,
- 12) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>S(O)O-2N(R<sup>46</sup>R<sup>47</sup>),
- 13) OS(O)O-2R<sup>61</sup>,
- 14) N(R<sup>46</sup>)C(O)R<sup>47</sup>,
- 15) N(R<sup>46</sup>)S(O)O-2R<sup>61</sup>,
- 16) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>N(R<sup>46</sup>)R<sup>61</sup>,
- 17) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>N(R<sup>46</sup>)R<sup>61</sup>OR<sup>47</sup>,
- 18) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>N(R<sup>46</sup>)(CR<sup>k</sup>R<sup>l</sup>)<sub>s</sub>C(O)N(R<sup>47</sup>R<sup>48</sup>),
- 19) N(R<sup>46</sup>)(CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>R<sup>61</sup>,
- 20) N(R<sup>46</sup>)(CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>N(R<sup>47</sup>R<sup>48</sup>),
- 21) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>C(O)N(R<sup>47</sup>R<sup>48</sup>), or
- 22) oxo, or

b) a heteroaryl ring selected from the group consisting of

- a 5-membered unsaturated monocyclic ring with 1, 2, 3 or 4 heteroatom ring atoms selected from the group consisting of N, O or S,
- a 6-membered unsaturated monocyclic ring with 1, 2, 3 or 4 heteroatom ring atoms selected from the group consisting N, O and S, and
- a 9- or 10-membered unsaturated bicyclic ring with 1, 2, 3 or 4 heteroatom ring atoms selected from the group consisting of N, O or S;

wherein any stable S heteroaryl ring atom is unsubstituted or mono- or di-substituted with oxo, and any stable C or N heteroaryl ring atom is independently unsubstituted or substituted with

- 1) halogen,
- 2) NO<sub>2</sub>,
- 3) CN,
- 4) CR<sup>46</sup>=C(R<sup>47</sup>R<sup>48</sup>)<sub>2</sub>,
- 5) C≡CR<sup>46</sup>,
- 6) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>OR<sup>46</sup>,
- 7) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>N(R<sup>46</sup>R<sup>47</sup>),
- 8) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>C(O)R<sup>46</sup>,
- 9) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>C(O)OR<sup>46</sup>,
- 10) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>R<sup>46</sup>,
- 11) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>S(O)<sub>0-2</sub>R<sup>61</sup>,
- 12) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>S(O)<sub>0-2</sub>N(R<sup>46</sup>R<sup>47</sup>),
- 13) OS(O)<sub>0-2</sub>R<sup>61</sup>,
- 14) N(R<sup>46</sup>)C(O)R<sup>47</sup>,
- 15) N(R<sup>46</sup>)S(O)<sub>0-2</sub>R<sup>61</sup>,
- 16) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>N(R<sup>46</sup>)R<sup>61</sup>,
- 17) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>N(R<sup>46</sup>)R<sup>61</sup>OR<sup>47</sup>,
- 18) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>N(R<sup>46</sup>)(CR<sup>k</sup>R<sup>l</sup>)<sub>s</sub>C(O)N(R<sup>47</sup>R<sup>48</sup>),
- 19) N(R<sup>46</sup>)(CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>R<sup>61</sup>,
- 20) N(R<sup>46</sup>)(CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>N(R<sup>47</sup>R<sup>48</sup>),
- 21) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>C(O)N(R<sup>47</sup>R<sup>48</sup>), or
- 22) oxo;

R<sup>1</sup> is selected from the group consisting of

- 1) hydrogen,

- 2)  $(CR_aR_b)_nR^{40}$
- 3)  $(CR_aR_b)_nOR^{40}$ ,
- 4)  $(CR_aR_b)_nN(R^{40}R^{41})$ ,
- 5)  $(CR_aR_b)_nN(R^{40})C(O)OR^{41}$ ,
- 6)  $(CR_aR_b)_nN(R^{40})(CR_cR_d)_2N(R^{41})C(O)R^{49}$ ,
- 7) C<sub>3-8</sub> cycloalkyl,
- 8)  $(CR_aR_b)_nC(O)OR^{40}$ ,
- 9)  $(CR_aR_b)_nN(R^{40})(CR_cR_d)_{1-3}R^{41}$ ,
- 10)  $(CR_aR_b)_nS(O)_{0-2}R^6$ ,
- 11)  $(CR_aR_b)_nS(O)_{0-2}N(R^{40}R^{41})$ ,
- 12)  $(CR_aR_b)_nN(R^{40})R^6OR^{41}$ ,
- 13)  $(CR_aR_b)_nN(R^{40})(CR_cR_d)_{0-6}C(O)N(R^{41}R^{42})$ ;

R<sub>5</sub> is selected from the group consisting of

- 1)  $C(O)N(R^{55}R^{50})$ ,
- 2)  $C(O)OR^{55}$ , and
- 3)  $C(O)R^{82}$ ;

R<sub>2</sub>, R<sub>8</sub>, R<sub>9</sub> and R<sub>10</sub> are independently selected from:

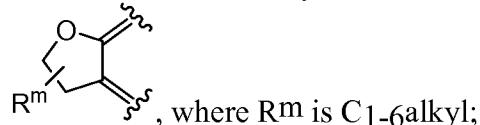
- 1) hydrogen,
- 2) halogen,
- 3) NO<sub>2</sub>,
- 4) CN,
- 5)  $CR^{43}=C(R^{44}R^{45})$ ,
- 6)  $C\equiv CR^{43}$ ,
- 7)  $(CRERF)_pOR^{43}$ ,
- 8)  $(CRERF)_pN(R^{43}R^{44})$ ,
- 9)  $(CRERF)_pC(O)R^{43}$ ,
- 10)  $(CRERF)_pC(O)OR^{43}$ ,
- 11)  $(CRERF)_pR^{43}$ ,
- 12)  $(CRERF)_pS(O)_{0-2}R^{60}$ ,
- 13)  $(CRERF)_pS(O)_{0-2}N(R^{43}R^{44})$ ,
- 14)  $OS(O)_{0-2}R^{60}$ ,
- 15)  $N(R^{43})C(O)R^{44}$ ,
- 16)  $N(R^{43})S(O)_{0-2}R^{60}$ ,
- 17)  $(CRERF)_pN(R^{43})R^{60}$ ,
- 18)  $(CRERF)_pN(R^{43})R^{60}OR^{44}$ ,
- 19)  $(CRERF)_pN(R^{43})(CRgRh)_qC(O)N(R^{44}R^{45})$ .

20) N(R<sub>43</sub>)(CRERF)<sub>p</sub>R<sub>60</sub>,

21) N(R<sub>43</sub>)(CRERF)<sub>p</sub>N(R<sub>44</sub>R<sub>45</sub>), and

22) (CRERF)<sub>p</sub>C(O)N(R<sub>43</sub>R<sub>44</sub>),

or R<sub>2</sub> and R<sub>8</sub> are independently as defined above, and R<sub>9</sub> and R<sub>10</sub>, together with the atoms to which they are attached, form the ring



R<sub>a</sub>, R<sub>b</sub>, R<sub>c</sub>, R<sub>d</sub>, R<sub>e</sub>, R<sub>f</sub>, R<sub>g</sub>, R<sub>h</sub>, R<sub>i</sub>, R<sub>j</sub>, R<sub>k</sub> and R<sub>l</sub> are independently selected from the group consisting of:

- 1) hydrogen,
- 2) C<sub>1</sub>-C<sub>6</sub> alkyl,
- 3) halogen,
- 4) aryl,
- 5) R<sub>80</sub>,
- 6) C<sub>3</sub>-C<sub>10</sub> cycloalkyl, and
- 7) OR<sup>4</sup>,

said alkyl, aryl, and cycloalkyl being unsubstituted, monosubstituted with R<sup>7</sup>, disubstituted with R<sup>7</sup> and R<sup>15</sup>, trisubstituted with R<sup>7</sup>, R<sup>15</sup> and R<sup>16</sup>, or tetrasubstituted with R<sup>7</sup>, R<sup>15</sup>, R<sup>16</sup> and R<sup>17</sup>.

R<sup>4</sup>, R<sub>40</sub>, R<sub>41</sub>, R<sub>42</sub>, R<sub>43</sub>, R<sub>44</sub>, R<sub>45</sub>, R<sub>46</sub>, R<sub>47</sub>, R<sub>48</sub>, R<sub>49</sub>, R<sub>50</sub>, R<sub>51</sub>, R<sub>52</sub>, and R<sub>55</sub> are independently selected from the group consisting of

- 1) hydrogen,
- 2) C<sub>1</sub>-C<sub>6</sub> alkyl,
- 3) C<sub>3</sub>-C<sub>10</sub> cycloalkyl,
- 4) aryl,
- 5) R<sub>81</sub>,
- 6) CF<sub>3</sub>,
- 7) C<sub>2</sub>-C<sub>6</sub> alkenyl, and
- 8) C<sub>2</sub>-C<sub>6</sub> alkynyl,

said alkyl, aryl, and cycloalkyl is unsubstituted, mono-substituted with R<sup>18</sup>, di-substituted with R<sup>18</sup> and R<sup>19</sup>, tri-substituted with R<sup>18</sup>, R<sup>19</sup> and R<sup>20</sup>, or tetra-substituted with R<sup>18</sup>, R<sup>19</sup>, R<sup>20</sup> and R<sup>21</sup>.

R<sub>6</sub>, R<sub>60</sub>, R<sub>61</sub>, and R<sub>62</sub> are independently selected from the group consisting of

1) C<sub>1</sub>-C<sub>6</sub> alkyl,

2) aryl,

3) R<sub>83</sub>, and

4) C<sub>3</sub>-C<sub>10</sub> cycloalkyl;

said alkyl, aryl, and cycloalkyl is unsubstituted, mono-substituted with R<sub>26</sub>, di-substituted with R<sub>26</sub> and R<sub>27</sub>, tri-substituted with R<sub>26</sub>, R<sub>27</sub> and R<sub>28</sub>, or tetra-substituted with R<sub>26</sub>, R<sub>27</sub>, R<sub>28</sub> and R<sub>29</sub>;

R<sub>7</sub>, R<sub>15</sub>, R<sub>16</sub>, R<sub>17</sub>, R<sub>18</sub>, R<sub>19</sub>, R<sub>20</sub>, R<sub>21</sub>, R<sub>26</sub>, R<sub>27</sub>, R<sub>28</sub>, and R<sub>29</sub> are independently selected from the group consisting of

1) C<sub>1</sub>-C<sub>6</sub> alkyl,

2) halogen,

3) OR<sub>51</sub>,

4) CF<sub>3</sub>,

5) aryl,

6) C<sub>3</sub>-C<sub>10</sub> cycloalkyl,

7) R<sub>84</sub>,

8) S(O)<sub>0-2</sub>N(R<sub>51</sub>R<sub>52</sub>),

9) C(O)OR<sub>51</sub>,

10) C(O)R<sub>51</sub>,

11) CN,

12) C(O)N(R<sub>51</sub>R<sub>52</sub>),

13) N(R<sub>51</sub>)C(O)R<sub>52</sub>,

14) S(O)<sub>0-2</sub>R<sub>62</sub>,

15) NO<sub>2</sub>, and

16) N(R<sub>51</sub>R<sub>52</sub>);

R<sub>80</sub>, R<sub>81</sub>, R<sub>82</sub>, R<sub>83</sub>, and R<sub>84</sub> are independently selected from a group of unsubstituted or substituted heterocyclic rings consisting of a 4-6 membered unsaturated or saturated monocyclic ring with 1, 2, 3 or 4 heteroatom ring atoms selected from the group consisting N, O and S, and a 9- or 10-membered unsaturated or saturated bicyclic ring with 1, 2, 3 or 4 heteroatom ring atoms selected from the group consisting of N, O or S; and

n, p, q, r, and s are independently 0, 1, 2, 3, 4, 5 or 6, and wherein said compound A compound of Claim 6, or a pharmaceutically acceptable salt thereof, is selected from the group consisting of

4-(3-fluorophenyl)-6-methoxy-n,n,2-trimethyl-1-oxo-1,2-dihydroisoquinoline-3-carboxamide,

4-(3-fluorophenyl)-6-methoxy-2-methyl-3-(pyrrolidin-1-ylcarbonyl)isoquinolin-1(2H)-one,

2-allyl-6-methoxy-1-oxo-4-phenyl-1,2-dihydroisoquinoline-3-carboxamide,

6-methoxy-2-methyl-4-phenyl-3-pyridin-2-ylisoquinolin-1(2h)-one,

2-cyclopropyl-6-methoxy-4-phenyl-3-(1,3-thiazol-2-yl)isoquinolin-1(2h)-one,

methyl 4-(3-fluorophenyl)-6-methoxy-2-methyl-1-oxo-1,2-dihydroisoquinoline-3-carboxylate,

methyl 6-methoxy-2-methyl-1-oxo-4-phenyl-1,2-dihydroisoquinoline-3-carboxylate,

7-methoxy-2-methyl-1-oxo-4-phenyl-1,2-dihydroisoquinoline-3-carboxylic acid,

methyl 7-methoxy-2-methyl-1-oxo-4-phenyl-1,2-dihydroisoquinoline-3-carboxylate, and  
ethyl 2-methyl-1-oxo-4-phenyl-1,2-dihydroisoquinoline-3-carboxylate.

8. (Withdrawn) A method of treating a condition in a mammal, the treatment of which is effected or facilitated by Kv1.5 inhibition, which comprises administering a compound of Claim 1 in an amount that is effective at inhibiting Kv1.5.

9. (Withdrawn) A method of Claim 8, wherein the condition is cardiac arrhythmia.

10. (Withdrawn) A method of Claim 9, wherein the cardiac arrhythmia is atrial fibrillation.

11. (Withdrawn) A method of Claim 9, wherein the cardiac arrhythmia is selected from the group consisting of atrial flutter, atrial arrhythmia and supraventricular tachycardia.

12. (Withdrawn) A method of preventing a condition in a mammal, the prevention of which is effected or facilitated by Kv1.5 inhibition, which comprises administering a compound of Claim 1 in an amount that is effective at inhibiting Kv1.5.

13. (Withdrawn) A method of Claim 12, wherein the condition is cardiac arrhythmia.

14. (Withdrawn) A method of Claim 13, wherein the cardiac arrhythmia is atrial fibrillation.

15. (Withdrawn) method of Claim 13, wherein the cardiac arrhythmia is selected from the group consisting of atrial flutter, atrial arrhythmia and supraventricular tachycardia.

16. (Withdrawn) A method of Claim 12, wherein the condition is a thromboembolic event.

17. (Withdrawn) A method of Claim 16, wherein the thromboembolic event is a stroke.

18. (Withdrawn) A method of Claim 12, wherein the condition is congestive heart failure.

19. (Currently Amended) A pharmaceutical formulation comprising a pharmaceutically acceptable carrier and the compound of Claim 4-7 or a pharmaceutically acceptable crystal form or hydrate thereof.

20. (Currently Amended) A pharmaceutical composition made by combining the compound of Claim 4-7 and a pharmaceutically acceptable carrier.

21. (Withdrawn) A method of treating cardiac arrhythmia comprising administering a compound of Claim 1 with a compound selected from one of the classes of compounds consisting of antiarrhythmic agents having Kv1.5 blocking activities, ACE inhibitors, angiotensin II antagonists, cardiac glycosides, L-type calcium channel blockers, T-type calcium channel blockers, selective and nonselective beta blockers, endothelin antagonists, thrombin inhibitors, aspirin, nonselective NSAIDs, warfarin, factor Xa inhibitors, low molecular

weight heparin, unfractionated heparin, clopidogrel, ticlopidine, IIb/IIIa receptor antagonists, 5HT receptor antagonists, integrin receptor antagonists, thromboxane receptor antagonists, TAFI inhibitors and P2T receptor antagonists.

22. (Withdrawn) A method for inducing a condition of normal sinus rhythm in a patient having atrial fibrillation, which comprises treating the patient with a compound of Claim 1.

23. (Withdrawn) A method for treating tachycardia in a patient which comprises treating the patient with an antitachycardia device in combination with a compound of Claim 1.